INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU03/01164

A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl. [7]: C12N 15/12, 15/52, 9/00, C07K 14/47, 16/18, 16/40, 16/42, G01N 33/48, 33/50, 33/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (IPC classification system followed by classification symbols)
SEE ABOVE

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
SEE BELOW

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
WPIDS, MEDLINE, CA (EDD, DD5, p53R2, CANCER, NEOPLASM, TUMOUR, HSP70, HRAS1, CHK2, CYCLIN, CDC2, BRCA, NAT1, IMPORTIN ALPHA, PROGESTIN)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Henderson, M. J., *et al*, The Journal of Biological Chemistry, (2002), 277 (29): 26468-26478. EDD, the human hyperplastic discs protein, has a role in progesterone receptor coactivation and potential involvement in DNA damage response. Whole document	27, 28, 32, 34, 43, 51-54
X	Honda, Y., *et al*, Journal of Biological Chemistry, (2002 Feb 1) 277 (5) 3599-605. Cooperation of HECT-domain ubiquitin ligase hHYD and DNA topoisomerase II-binding protein for DNA damage response. Abstract; Introduction; Page 3600, col 2 lines 20-24, 37-40.	27, 37, 38, 43, 46, 51-54,

[X] Further documents are listed in the continuation of Box C [ ] See patent family annex

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
12 December 2003	18 DEC 2003
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized officer CHRIS LUTON Telephone No : (02) 6283 2256

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C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Callaghan, M.J., *et al*, Oncogene (1998 Dec 31) 17 (26) 3479-91. Identification of a human HECT family protein with homology to the Drosophila tumor suppressor gene hyperplastic discs. Whole document	1-13, 37-39
X	Richter, J., *et al*, Cancer Research, (1999 Nov 15) 59 (22) 5687-91. Chromosomal imbalances are associated with a high risk of progression in early invasive (pT1) urinary bladder cancer. Introduction col 2, Table 1	1-5, 12
X	Tosi, S., *et al*, Genes, Chromosomes and Cancer, (1999 Mar) 24 (3) 213-21. Characterization of the human myeloid leukemia-derived cell line GF-D8 by multiplex fluorescence in situ hybridization, subtelomeric probes, and comparative genomic hybridization. Abstract; Introduction; Table 1; page 219, col 1 lines 9,10; page 220 col 2 lines 30-33.	1-5, 12
X	Forozan, F., *et al*, British Journal of Cancer, (1999 Dec) 81 (8) 1328-34. Molecular cytogenetic analysis of 11 new breast cancer cell lines. Abstract; page 131, col 2, lines 5-7; page 1332, col 1, lines 8-12; page 1333, col 1, lines 9-21.	1-5, 12
X	Larramendy, M. L., *et al*, Cancer Genetics and Cytogenetics, (2000 Jun) 119 (2) 132-8. Comparative genomic hybridization reveals complex genetic changes in primary breast cancer tumors and their cell lines. Abstract; Table 1- HCC38, HCC 1739, HCC1954; page 135, col 2, lines 10-13; page 136,col 2, lines 1-10; page 137, col 1 last 5 lines.	1-5, 12
PX	Clancy, J. L., *et al*, Oncogene, (2003 Aug 7) 22 (32) 5070-81. EDD, the human orthologue of the hyperplastic discs tumour suppressor gene, is amplified and overexpressed in cancer. Whole document	1-26

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Box I **Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos :

because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos : **63-74**

because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

Claims 63-74, relate to agents that modulate EDD, the claims were only searched as they relate to the use of derivatives of EDD, eg ribozymes, siRNA, antibodies etc that are based on the EDD sequence. This is because the claims that include the use of other unspecified agents that are not necessarily derived from the EDD, are not limited to the technical features of the invention.

3. ☐ Claims Nos :

because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

Box II **Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

The application claims more than one invention. (see continuation of Box II)

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☒ No protest accompanied the payment of additional search fees.

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Supplemental Box
(To be used when the space in any of Boxes I to VIII is not sufficient)

Continuation of Box No: II

The claims define 24 inventions. The inventions fall into two broad categories.

Category 1

Claims 1-26 and 63-74 broadly define methods of detecting cancer by assessing the expression of nucleic acids at locus 8q22.3. Narrower dependent claims define detection of EDD and/or p53R2 at 8q22.3

Methods of cancer detection at 8q22.3, therefore there are two inventions:

i. Detection of cancer comprising assessing levels of EDD.
ii. Detection of cancer comprising assessing levels of p53R2.

Category 2

Claims 27-62 define peptide complexes comprising EDD and cell cycle modulatory (eg topIIb), tumour suppressor (eg progesterone receptor), nuclear targeting (eg importin alpha 5) or DNA damage or repair peptides (eg calcium and integrin binding protein).

Although the claims share a feature of peptide complexes comprising EDD, this feature is known, see Henderson *et al.* Furthermore, even if claims were to be divided into inventions relating to complexes comprising EDD and cell cycle modulatory (1), nuclear targeting (2), DNA damage or repair (3), tumour suppressor (4), these features are also known, see Henderson *et al* or Honda *et al.*
Therefore, there are at least 22 different inventions consisting of complexes of EDD and:
CDS1, p53(TP53), TNF-alpha, HSP70, estrogen receptor, androgen receptor, progesterone receptor (SEQ ID NO 15), HRAS1-VNTR, CHK2 (SEQ ID NO 19), BRCA1, BRCA2 (SEQ ID NO 23), AIB1, NAT1, NAT2, XRCC1, XRCC2, XRCC5, CIB (SEQ ID NO 17), importin alpha 1 (SEQ ID NO 9), importin alpha 2 (SEQ ID NO 11), importin alpha 3 (SEQ ID NO 13), cdc25, cdc2a, cyclin-dependent kinase (cdk), cdk-inhibitor, mitogenic cyclins (A, B, C, D etc), MLH1, MSH2, and ATM.

In total, there are at least 22 inventions in category 2. Although some of the alternatives listed can be grouped together ie importins alpha 1, 2 and 3, independent members of some of these groups are known as complexes with EDD, thereby leading to lack of unity within the group.